Non-Technical Abstract

Patients with certain genetic and malignant diseases may benefit from the transplantation of hematopoietic (blood forming) stem cells following chemotherapy and radiation. Stem cells have traditionally been obtained from the bone marrow, but more recently investigators have studied the potential use of stem cells obtained from the placenta and umbilical cord of newborn infants as an alternate source of stem cells suitable for transplantation. Preliminary studies at Indiana University and elsewhere have suggested that while cord blood is capable of forming new bone marrow and blood in a portion of patients, failure of these cells to grow (non-engraftment) may be problematic. In addition, the rate of new blood formation appears to be slower than that expected from stem cell obtained from bone marrow. An additional concern is that a unit of cord blood may not contain enough stem cells to reliably engraft larger recipients. In attempts to address these issues, investigators at Indiana University and the University of Colorado are currently conducting studies utilizing new technologies for stem cell selection and expansion of stem cells in the laboratory (*ex vivo*). This study will determine if the transplantation of cord blood stem cells that have a new gene derived from a bacteria inserted into them and manipulated in the laboratory for 10 days prior to transplantation are safe and if they are able to grow and contribute to new bone marrow and blood formation. For patients whose cord blood unit is divided into two aliquots (either 50%/50% or 60%/40%), at the time of cryopreservation, an aliquot (50% or 60%) of the unit will be infused, unmanipulated, on Day 0. The other aliquot (50% or 40%) will be selected, transduced and expanded, then infused on day +10. For all cord blood units frozen in a single bag, 60% will be infused, unmanipulated, on Day 0. The remaining 40% will be selected, transduced and expanded, then infused on day +10. The new gene is inserted using special viruses (retroviruses) that infect stem cells. Entry of the virus is enhanced by using a natural protein (fibronectin fragments) and growth factors. The cells that have the new gene inserted are then expanded in the laboratory using the same growth factors. Patients will be assessed for infusion related toxicities as well as for the presence of replication competent retrovirus (RCR). Transfer of the retroviral genetic material will be determined in blood and bone marrow at various time points. This study will enroll 10 patients. The study will be stopped for unacceptable toxicity that is defined in the protocol.